Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1-44. (canceled)

45. (new) A method for detecting a variation in *GH1* effective to act as an indicator of GH dysfunction in an individual, wherein said method comprises the steps of:

(a) obtaining a test sample comprising a nucleotide sequence of human *GH1* gene from said individual;

(b) examining the sequence obtained from the test sample to identify any test sample variants;

(c) if a test sample variant is identified, comparing test sample variant with a variant in Table 7B herein and where it is determined that one or more of said variant in Table 7B is, or are, present in said test sample;

(d) concluding that said test sample variant is an effective indicator of growth hormone dysfunction wherein the test sample is obtained from an individual exhibiting the following criterion:

(i) growth failure, defined as a growth pattern which, when plotted on a standard height chart, predicts an adult height for the individual which is outside the individual's estimated target

adult height range, the estimate being based upon the heights of the individual's parents.

46. (new) A method according to claim 45, wherein the test sample is obtained from an individual exhibiting at least one of the following further criteria:

(ii) height velocity below the 25th centile for age; and/or

(iii) bone age delay of at least two years when compared with chronological age; and/or

(iv) no other disorder known to cause inclusion in criteria (i) to (iii) above.

47. (new) A method according to claim 46, wherein the bone age delay is in the range of from 2 to 4 years, when compared with chronological age.

48. (new) A method according to claim 45, wherein the individual exhibits normal results in a standard growth hormone secretion test.

49. (new) A method according to claim 45, wherein the method comprises any sequencing method for determining the sequence of the *GH1* gene of an individual.

50. (new) A method according to claim 45, wherein the method comprises PCR amplification of the *GH1* gene of the individual using (a) a *GH1* gene-specific fragment, being a fragment unique to the *GH1* gene whose sequence is not found in four other paralogous genes in the GH cluster selected from the

group consisting of *CSH1*, *CSH2*, *CSHP1* and *GH2*, and (b) one or more *GH1* gene-specific primers which cannot bind to homologous flanking regions in the four other paralogous non-*GH1* genes in the GH cluster.

51. (new) A method according to claim 45, wherein the method comprises PCR amplification of the entire *GH1* gene of the individual and nested PCR of overlapping constituent fragments of the *GH1* gene of the individual.

52. (new) A method according to claim 45, wherein the method comprises PCR amplification of all or a fragment of genomic DNA spanning the Locus Control Region of the *GH1* gene.

53. (new) A method according to claim 45, wherein the method comprises mutational screening of all or a fragment of the individual's *GH1* gene by DHPLC.

54. (new) A detection method according to claim 45, further determining the sequence of said test nucleotide sequence with a primer selected from the group consisting of:

CTC CGC GTT CAG GTT GGC (GH1DF) (SEQ ID NO. 37);

AGG TGA GCT GTC CAC AGG (GH1DR) (SEQ ID NO. 38);

GGG CAA CAG TGG GAG AGA AG (GH2DF) (SEQ ID NO. 39);

CCT CCA GGG ACC AGG AGC (GH2DR) (SEQ ID NO. 40);

CAT GTA AGC CCA GTA TTT GGC C (GH3DF) (SEQ ID NO. 41);

CTG AGC TCC TTA GTC TCC TCC TCT (GH3DR) (SEQ ID NO. 42);

GAC TTT CCC CCG CTG GGA AA (GH4DF) (SEQ ID NO. 43);

GGA GAA GGC ATC CAC TCA CGG (GH4DR) (SEQ ID NO. 44);

TCA GAG TCT ATT CCG ACA CCC (GH5DF) (SEQ ID NO. 45);

GTG TTT CTC TAA CAC AGC TCT C (GH5DR) (SEQ ID NO. 46);

TCC CCA ATC CTG GAG CCC CAC TGA (GH6DF) (SEQ ID NO. 47);

CGT AGT TCT TGA GTA GTG CGT CAT CG (GH6DR) (SEQ ID NO. 48);

TTC AAG CAG ACC TAC AGC AAG TTC G (GHD7F) (SEQ ID NO. 49);

CTT GGT TCC CGA ATA GAC CCC G (GH7DR) (SEQ ID NO. 50);

GTGCCCCAAGCCTTTCCC (LCR15: 1159-1177) (SEQ ID NO. 55);

TGTCAGATGTTCAGTTCATGG (LCR13: 1391-1412) (SEQ ID NO. 56);

CCTCAAGCTGACCTCAGG (LCR25: 1346-1363) (SEQ ID NO. 57);

GATCTTGGCCTAGGCCTCG (LCR23: 1584-1602) (SEQ ID NO. 58);

LCR 5A (5′ CCAAGTACCTCAGATGCAAGG 3′) (SEQ ID NO. 24);

LCR 3.0 (5′ CCTTAGATCTTGGCCTAGGCC 3′) (SEQ ID NO. 25);

LCR 5.0 (5′ CCTGTCACCTGAGGATGGG 3′) (SEQ ID NO. 26);

LCR 3.1 (5′ TGTGTTGCCTGGACCCTG 3′) (SEQ ID NO. 27);

LCR 3.2 (5′ CAGGAGGCCTCACAAGCC 3′) (SEQ ID NO. 28);

LCR 3.3 (5′ ATGCATCAGGGCAATCGC 3′) (SEQ ID NO. 29);

GH1G5 (5' GGTACCATGGCTACAGGTAAGCGCC 3') (SEQ ID NO. 30);

GH1G3 (5' CTCGAGCTAGAAGCCACAGCTGCCC 3') (SEQ ID NO. 31);

BGH3 (5' TAGAAGGCACAGTCGAGG 3') (SEQ ID NO. 59);

GH1F (5′ GGGAGCCCCAGCAATGC 3′) (SEQ ID NO. 35);

GH1R (5′ TGTAGGAAGTCTGGGGTGC 3′) (SEQ ID NO. 36);

GH1R5 (5' ATGGCTACAGGCTCCCGG 3') (SEQ ID NO. 60); and

GH1R3 (5' CTAGAAGCCACAGCTGCCC 3') (SEQ ID NO. 61).

55. (new) A *GH1* variant comprising any one or more of said variants in Table 7B herein.

56. (new) A screening method for identifying an individual with GH dysfunction, wherein said screening method comprises the steps of:

(a) obtaining a test sample comprising a nucleotide sequence of the human *GH1* gene from the individual; and

(b) comparing a region of the sequence obtained from the test sample with the same region of a *GH1* sequence that includes at least one of said variants in Table 7B; and

(c) if said test sample nucleotide sequence is shown to contain one of said variants in Table 7B, concluding GH dysfunction is present

57. (new) A screening method according to claim 56, wherein the test sample comprises genomic DNA.

58. (new) A screening method for screening an individual suspected of GH dysfunction, which screening method comprises the steps of:

(a) obtaining a test sample comprising a nucleotide sequence of the human *GH1* gene or an amino acid sequence encoded thereby from the individual; and

(b) analysing the test sample for the presence of a variant of *GH1* or a GH variant or for the presence of one or more surrogate

markers that are indicative of or correlated to the presence of a variant of *GH1* or a GH variant,

wherein the variant of *GH1* or the GH variant exhibits at least one variation when compared to the wild type hGH sequence and is obtainable from a second test sample derived from an individual exhibiting the following criterion:

(i) growth failure defined as a growth pattern which, when plotted on a standard height chart, predicts an adult height for the individual which is outside the individual's estimated target adult height range, the estimate being based upon the heights of the individual's parents.

59. (new) A screening method according to claim 56, comprising:

(a) obtaining a transcript of said test sample nucleotide sequence; and

(b) comparing said transcript with a transcript of *GH1* shown in Table 7B herein in order to determine whether any of the transcript variants shown in Table 7B exist in said test sample transcript; and

(c) where at least one of said transcript variants of Table 7B is found in said test sample transcript concluding GH dysfunction is present.

60. (new) A screening method according to claim 56, wherein part (b) thereof involves comparing multiple regions of

said test sample nucleotide sequence with multiple regions of said same sequences with a view to identifying at least one of said novel variants in Table7B wherein said method involves:

i) hybridisation of a labelled sample of DNA derived from the individual micro-array of variant-specific oligonucleotide probes which are immobilised on a solid support.